AMENDMENTS TO THE DRAWINGS

The attached sheet is a replacement sheet for Figure 3 .

Attachment: Replacement sheet (Figure 3)

REMARKS

Claims 22 and 49 are currently pending in the application and have been amended. Claims 1-21, 23-48 have been canceled without prejudice. No new matter has been added by this amendment.

Applicants respectfully reserve the right to pursue any non-elected, canceled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

It is submitted that the claims, herewith and as originally presented were in full compliance with the requirements of 35 U.S.C. § 112. The amendment of the claims, as presented herein, is not made for purposes of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, this amendment is made simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that the herewith amendment should not give rise to any estoppel.

Reconsideration and withdrawal of the rejections of this application in view of the amendments and remarks herewith, is respectfully requested, as the application is in condition for allowance.

The specific grounds for rejection and Applicant's response to them are set forth in detail below:

1. The drawing of Figure 3 is objected to because each of the panel is still black.

Applicant is concurrently submitting a "Replacement Sheet" for Figure 3 of the application. The Examiner is requested to please see the "Attachment". The "Replacement Sheet" contains discernable data therein.

2. Claims 22 and 49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis of this rejection is set forth for claims 22 and 23 at page 3 of the previous Office action of 29 June 2007.

The Examiner states, "The rejection of claim 22 and the newly added claim 49 is maintained. Applicant's response and arguments filed on 09/24/2007 have been fully considered but they are not persuasive.

Applicant argues that the claims have been amended such that the SGLT homolog is limited to a protein which comprises the amino acid sequence represented by SEQ ID NO:1 or having an amino acid sequence having at least about 90% homology to the amino acid sequence represented by SEQ ID NO:1, its partial peptide, or a salt thereof. Furthermore, the claimed method has been amended to recite specific steps Applicant's claim amendments have been fully considered but are not found persuasive. The amendments of claim 22 do not satisfy the written description requirement because the claim language "...an amino acid sequence having at least about 90% homology to the amino acid sequence represented by SEQ ID NO: 1, ...its partial peptide, or a salt thereof' has been broadly interpreted by the Examiner as encompassing any variants, fragments and mutants of the SGLT homolog of SEQ ID NO: 1.

To provide adequate written description and evidence of possession of claimed genus, the specification must provide efficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure/function correlation, and other identifying characteristics. Accordingly, in the absence of sufficient recitation of distinguishing structural/physical and identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Applicant recites general characteristics regarding a "Na-f•/glucose transporter (SGLT) homolog" without any sufficient recitation of distinguishing structural/physical and identifying characteristics of an amino acid sequence having at least about 90% homology to the amino acid sequence represented by SEQ ID NO:1 or fragments thereof. For instance, the claims do not disclose any identifying structural or functional characteristics of a SGLT homolog having at least about 90% homology to the amino acid sequence represented by SEQ ID NO:1 or its partial peptide. While Applicant discloses the general functional characteristics of a SGLT homolog, Applicant has not provided any specific identifying structural characteristics so that one skilled in the art can correlate a SGLT homolog having at least about 90% homology to the amino acid sequence represented by SEQ ID NO:1 or its partial peptide with a distinct biological function. At page 8, the specification teaches that the Na^{y}-/glucose transporter (SGLT) homologs may be any protein derived from any cells of human and warm-blooded animals ... (page 8 lines 23-25). However, the specification does not teach any variants of a SGLT

homolog having at least about 90% homology to the amino acid sequence represented by SEQ ID NO:1 or fragments thereof that can regulate glucose uptake activity. At page 8, the specification does not provide sufficient teachings correlating the structure of a variant of a SGLT homolog with its biological function, so that one skill in the art can identify the claimed SGLT homolog of the instant application.

There is no description of the conserved regions, which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the variants of SGLT homolog having at least about 90% homology to the amino acid sequence represented by SEQ ID NO:1 or fragments thereof encompassed by the claims. Thus, no identifying characteristics or properties of the instant variants, fragments, and mutants of the isolated protein consisting of a SGLT homolog having at least about 90% homology to the amino acid sequence represented by SEQ ID NO:1 are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Additionally, the broad brush discussion of making and screening for variants does not constitute a disclosure of a representative number of members. No such variants were made or shown to have activity. Only the polypeptide of SEQ ID NO:1 is disclosed. The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed variants. The specification does not provide any disclosure regarding the number of amino acid changes, the identities of the amino acids and the location of these changes for the claimed polypeptide variants while still retaining a biological function."

Applicants respectfully disagree. The Examiner alleges that the claim language "... an amino acid sequence having at least about 90% homology to the amino acid sequence represented by SEQ ID NO: 1, ... its partial peptide, or a salt thereof" has been broadly interpreted by the Examiner as encompassing any variants, fragments and mutants of the SGLT homolog of SEQ ID NO: 1, and thus claim 22 do not satisfy the written description requirement.

In the attached amended claims, the claim language "an amino acid sequence having at least 90% homology to the amino acid sequence represented by SEQ ID NO: 1, ... its partial peptide, or a salt thereof" has been deleted.

The amended claim 22 recites a method of screening a compound or its salt that regulates the glucose uptake activity of a Na^+/glucose transporter homolog in the small intestine, which comprises:

determining (i) the glucose uptake activity of a cell expressing the homolog in the absence of a test compound and (ii) the glucose uptake activity of a cell expressing the homolog in the presence of a test compound, wherein the cell is present in a jejunal slice in an intestinal organ culture system,

comparing the glucose uptake activities, and

selecting a test compound that promotes or inhibits the glucose uptake activity,

wherein the homolog is a protein which comprises the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 50 and has an active glucose transport activity, or a salt thereof. A protein which comprises the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5 or SEQ ID NO: 50 and has an active glucose transport activity is specifically described in the present specification (see, for example, Examples 1, 7-9, 11). Given the amendments to the claims and the specific limitations to certain SEQ ID NOS, Applicants respectfully request reconsideration.

3. Claims 22 and 49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening a compound that suppresses the glucose uptake activity of the SGLT homolog comprising the amino acid sequence of SEQ ID NO:1, does not reasonably provide enablement for a method of screening a compound that regulates the glucose uptake activity of a Na+/glucose transporter (SGLT) homolog or a protein comprising the same of substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO:1 in the small intestine comprising the homolog. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention

commensurate in scope with these claims. The basis of this rejection is set forth for claims 22 and 23 at page 6 of the previous Office action of 29 June 2007.

> The Examiner states "The rejection of claim 22 and the newly added claim 49 is maintained. Applicant's response and arguments filed on 09/24/2007 have been fully considered but they are not persuasive.
>
> Applicant's claim amendments have been fully considered but are not found persuasive. The amendments of claim 22 do not satisfy the enablement requirement because the claimed method requires undue experimentation.
>
> As disclosed above and at page 8 of the Office action mailed 06/29/2007, the invention is broad because the recitation of claim 22 encompasses a large number of polypeptides.
>
> Specifically, the Examiner has broadly interpreted the recitation in claim 22 of "...an amino acid sequence having at least about 90% homology to the amino acid sequence represented by SEQ ID NO: 1, ...its partial peptide, or a salt thereof' as encompassing any variants, fragments and mutants of the SGLT homolog of SEQ ID NO: 1. It would require undue experimentation by one skilled in the art to be able to practice the invention commensurate in scope with the claims because the claims are broadly drawn to a method comprising the variants and fragments of a SGLT homolog having at least about 90% homology to the amino acid sequence represented by SEQ ID NO:1.
>
> In addition, it would require undue experimentation for one of skill in the art to be able to screen a compound or its salt that regulates the glucose uptake activity of a Na^+/glucose transporter (SGLT) homolog in the small intestine without sufficient disclosure in the specification regarding the functional characteristics of a SGLT homolog having at least about 90% homology to the amino acid sequence represented by SEQ ID NO:1 and fragments thereof.
>
> Finally, it would require undue experimentation for one of skill in the art to be able to screen a compound that regulates the glucose uptake activity of a Na+/glucose transporter (SGLT) homolog having at least about 90% homology to the amino acid sequence represented by SEQ ID NO:1. Although Applicant has provided guidance regarding the polypeptide of SEQ NO:1 (page 9, lines 6-15), the specification does not teach any polypeptide variants at least 90% identical to SEQ ID NO:1 or fragments thereof required in order to maintain its biological activity as a glucose transporter. In addition, the specification does not provide any disclosure regarding the number of amino acids changes, the identities of the amino acids and the location of these changes for the claimed polypeptide variants while still

retaining a biological function. It is well known in the art that certain amino acid positions in the sequence are critical to the proteins structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the three-dimensional spatial orientation of binding and active sites (see for example, Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495; Bork, 2000, Genome Research 10:398-400; Skolnick et al., 2000, Trends in Biotech. 18(1):34-39, especially p. 36 at Box 2; Doerks et al., 1998, Trends in Genetics 14:248-250; Smith et al., 1997, Nature Biotechnology 15:1222-1223; Brenner, 1999, Trends in Genetics 15:132-133; Bork et al., 1996, Trends in Genetics 12:425-427).

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

In view of these teachings in the art and the limited guidance provided in the specification, a method of screening a compound that suppresses the glucose uptake activity of SGLT homolog of SEQ ID NO:1 is not predictable for a method of screening a compound that regulates the glucose uptake activity of a Na-F/glucose transporter (SGLT) homolog or a protein comprising the same of substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO:1 in the small intestine comprising the homolog."

Applicants respectfully disagree. The Examiner indicates that the specification, while being enabling for a method of screening a compound that suppresses the glucose uptake activity of the SGLT homolog comprising the amino acid sequence of SEQ ID NO: 1, does not reasonably provide enablement for a method of screening a compound that regulates the glucose uptake activity of a Na^+/glucose transporter (SGLT) homolog or a protein comprising the same

of substantially the same amino acid sequence as the amino acid sequence represented by SEQ ID NO; 2 in the small intestine comprising the homolog.

As shown in the attached amended claims, claim 22 has been amended to limit the homologs to those comprising the amino acid sequence of SEQ ID NO: 3, 5 or 50. The present specification describes that these homologs have equivalent activity as the homolog of SEQ ID NO: 1 (see, for example, page 37, Examples 1, 7, 11, etc.). Thus, the present specification reasonably provides enablement for a method as claimed in the amended claim 22. Once again, given the amendments to the claims and the specific limitations to certain SEQ ID NOS, Applicants respectfully request reconsideration.

4. Claims 22 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention.

> The Examiner states "Although Applicants have overcome the previous rejection under 35 USC 112, 2nd paragraph by amending claim 22, the amendments made to claim 22 and the addition of claim 49 have raised new issues under 35 USC 112, 2nd paragraph.
>
> a. The phrase "a cell capable of producing the homolog" in claim 22, line 4 is a relative term which renders claim 22 indefinite. The term "a cell capable of producing the homolog" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For instance, it is not clear that the homolog is definitely expressed by the cell. (Please note that this issue could be overcome by amending the claim to recite, for example, "...a cell expressing the homolog...".
>
> b. The phrase "a mixture of cell capable of producing the homolog and a test compound" in claim 22, lines 5-6 is a relative term which renders claim 22 indefinite. The term "a mixture of cell capable of producing the homolog and a test compound" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For instance, it is not clear if the homolog and the test compound are both

being expressed by the cell or if the compound is added to a cell expressing the homolog. (Please note that this issue could be overcome by amending the claim to recite, for example, "..a cell expressing the homolog in the presence of a test compound...".)

c. The term "cases" in claims 22 and 49 is a relative term which renders the claims 22 and 49 indefinite. The term "cases" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For instance, it is not clear as to what is encompassed by the recitation of cases. Is the term "cases" intended to mean "steps"?

d. Claims 22 and 49 are indefinite because the claims have a step that does not clearly relate back to the preamble. For example, the preamble of claim 22 recites "a method of screening a compound or its salt that regulates the glucose uptake activity of a Na^+/glucose transporter (SGLT) homolog in the small intestine". However, there is no step in the body of the claim indicating that the regulation of the glucose uptake activity of a Na^+/glucose transporter has taken place.

e. Claim 49 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. For instance, it is not clear as to how the measurements for the accumulation of glucose analogs are determined in the claimed method. Lines 3-4 of claim 49 are particularly confusing. For example, it is not clear if radioactivity is being measured or the presence of the accumulated analogs."

Applicants respectfully disagree. The Examiner alleges that claims 22 and 49 are rejected as being indefinite.

a. The Examiner states that the phrase "a cell capable of producing the homolog" in claim 22, line 4 renders claim 22 indefinite, and suggested that this issue could be overcome by amending the claim to recite "... a cell expressing the homolog...".

As shown in the claim amendments, claim 22 has been amended to recite "... a cell expressing the homolog..." as suggested by the Examiner.

b. The Examiner states that the phrase "a mixture of cell capable of producing the homolog and a test compound" in claim 22, lines 5-6 renders claim 22 indefinite, and suggested that this issue could be overcome by amending the claim to recite "... a cell expressing the homolog in the presence of a test compound ...".

As shown in the claim amendments, claim 22 has been amended to recite "... a cell expressing the homolog in the presence of a test compound ..." as suggested by the Examiner.

c. The Examiner states that the term "cases" in claims 22 and 49 renders the claims 22 and 49 indefinite.

As shown in the claim amendments, claims 22 and 49 have been amended to delete the term "cases" and clarify what is claimed in the claims.

d. The Examiner alleges that claims 22 and 49 are indefinite because the claims have a step that does not clearly relate back to the preamble.

As shown in the claim amendments, a step of "selecting a test compound that promotes or inhibits the glucose uptake activity" has been added in claim 22. This step relate back to the preamble of claim 22, which recites "a method of screening a compound or its salt that regulates the glucose uptake activity of a Na^+/glucose transporter (SGLT) homolog in the small intestine".

e. The Examiner alleges that claim 49 is indefinite because it is not clear if radioactivity is being measured or the presence of the accumulated analogs.

As shown in the claim amendments, claim 49 has been amended to clarify that the glucose uptake activities are determined by measuring the amount of glucose analogs, which are labeled with radioactivity, accumulated in the cells by counting the radioactivity. Applicants respectfully request reconsideration.

5. Claims 22 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Iwamoto et al. (WO 02/053738; priority to the publication date of July 11, 2002, cited in the IDS filed 04/28/2005). The basis of this rejection is set forth for claims 22 and 23 at page 14 of the previous Office action of 29 June 2007.

> The Examiner states "The rejection of claim 22 and the newly added claim 49 under 35 USC 102 (b) is maintained. Applicant's response and arguments filed on 09/24/2007 have been fully considered but they are not persuasive.
>
> At page 14 of the response, Applicant argues that no reference discloses, teaches, or suggests a method of screening a compound or its salt that regulates the glucose uptake activity of a Na+/glucose (SGLT) homolog in the small intestine, and thus the present invention is novel and would not be obvious over the cited references.
>
> Applicant's claim amendments have been fully considered but are not found persuasive. Iwamoto et al., (2002) teach a method of screening a compound regulating glucose uptake activity using the homolog (page 36, lines 19-29) comprising SEQ ID NO:1 (abstract page 1 and page 1 of sequence listing), which has 100% homology with SEQ ID NO:1 of instant application.
>
> In addition, Iwamoto et al. (2002) teach a method of screening for the compound comprising comparing (i) glucose uptake activity in cells having the ability of producing the protein and (ii) glucose uptake activity in cells having the ability of producing the protein in the presence of the test compound (page 36, lines 15-30). These teachings meet the limitations of claim 22.
>
> Finally, Iwamoto et al. (2002) teach that the glucose activity of the method is determined by measuring radioactivity of the intracellular accumulation of [3H1-labeled glucose or glucose analogs, such as 2-deoxy-glucose (page 36, lines 23-30) meeting the limitations of claim 49."

Applicants respectfully disagree. Applicants believe that given the amendments to claims 22 and 49, the basis for this rejection is obviated. Specifically, claim 22 has been amended to clarify that the cell used in the step of claim 22 is present in a jejunal slice in an intestinal organ culture system. Support for this amendment can be found in Example 7, etc. of the present specification.

No references disclose, teach, or suggest a method of screening a compound or its salt that regulates the glucose uptake activity of a Na^+/glucose (SGLT) homolog in the small intestine, wherein a cell present in a jejunal slice in an intestinal organ culture system is used in the method. Applicants respectfully request reconsideration.

6. Claim 22 is rejected under 35 U.S.C. 102(b) as being anticipated by Thornton et al. (WO 01/92304 A2; priority to the publication date of May 25, 2001).

> The Examiner states "As disclosed in the previous Office action, Thornton et al., (2001) teach a method of screening a compound regulating glucose uptake activity using the homolog (page 16, lines 19). In addition, Thornton et al (2001) recite that the method of screening a compound comprises SEQ ID NO:20 (page 16, line 3 and page 31 of sequence listing), which has 97.6% homology with SEQ ID NO:1 of the instant application (see alignment in Exhibit C of the previous Office Action of June 29, 2007) meeting the limitations of claim 22. It is noted that the Examiner has interpreted the phrase "an amino acid sequence having at least about 90% homology to the amino acid sequence represented by SEQ ID NO: 1" in the instant claims as reading upon variants, derivatives, and fragments of a SGLT homolog of the amino acid sequence of SEQ ID NO:1.
>
> Finally, Thornton et al. teach that the method comprises combining the polypeptide with at least one test compound under conditions permissive for the activity of the polypeptide, b) assessing the activity of the polypeptide in the presence of the test compound, and c) comparing the activity of the polypeptide in the presence of the test compound with the activity of the polypeptide in the absence of the test compound, wherein a change in the activity of the polypeptide in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide (page 17, lines 10-15). The teachings by Thornton et al. meet the limitations of claim 22."

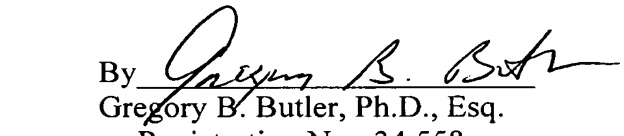
Applicants respectfully disagree. Applicants believe that given the amendments to claims 22 and 49, the basis for this rejection is obviated. For the same reasons cited against the Iwamoto reference, Applicants respectfully request reconsideration.

CONCLUSION

In view of the remarks made herein, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. Please charge any required fee or credit any overpayment to Deposit Account No. 04-1105.

Dated: September 3, 2008

Respectfully submitted,

By 

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Attachments